ATTACHE: Chemotherapy given before and after operation for secondary bowel cancer in the liver or given only after the operation

The ATTACHE trial aimed to answer an important health question: to provide evidence on the timing of chemotherapy for treating cancer of the bowel that has spread to the liver.

We appreciate the part played by our volunteer participants. This may help to improve the medical treatment of patients in the future. Here is a summary of the trial and results.

What was the trial about?

When bowel cancer spreads, it most commonly goes to the liver. The secondary cancers in the liver are removed by surgery. However, this does not stop the disease in two-thirds of patients. Therefore, chemotherapy treatment may be given, sometimes before and after the operation and sometimes only afterward.

In the ATTACHE trial, patients were randomly allocated to chemotherapy for 3 months before and another 3 months after their operation or to one course of chemotherapy for 6 months after their operation.

The investigators intended to enrol 200 participants, but had great difficulty recruiting them. After 8 people had been recruited, the investigators decided to stop and analyse the results together with the results of 2 similar overseas trials that had also had not been able to recruit enough participants. The other trials were EPOC B in the UK, and C-11 in the USA.

There were 28 patients overall. More than half were men. The average age was 68, but their ages ranged from 33 to 81. They all had cancer that had spread to the liver, but had not been disabled by the disease and most were well enough to work.

How was the effect of treatment measured?

The main measure of success in ATTACHE was the proportion of patients who had complications of surgery. Fewer complications can indicate that the chemotherapy is more beneficial or less harmful.

In the combined analysis of the 3 trials, the researchers also measured the proportion of patients who completed their chemotherapy as planned, the adverse events (that is, symptoms and abnormal test results that may or may not have been related to the treatment), and the patients' quality of life.

The researchers also measured progression-free survival—that is, the time between the participant's entry into the trial until the disease became worse—and their survival overall.

Which treatment was better?

It appeared that the group who had all their chemotherapy after operation had fewer surgical complications. But even by combining the 3 trials, there were not enough participants to analyse the data properly.

What were the side-effects of the treatment?

In all 3 trials analysed together, the most common problems were abnormal blood counts. Some participants had fever, diarrhoea, vomiting, or numbness. There were also events that were considered to be due to the operation, such as infections, bowel obstruction, hernia, blood clots and heart or lung disturbances.

The numbers of patients were too small to know if one treatment had significantly more disorders than the other.

Were there any serious side-effects?

Eight patients had a serious event that required hospital treatment, including bowel obstruction, severe vomiting, a blood clot in the lung, and stomach pain. These were all well understood events and could have been due to the operation, the chemotherapy treatment, or the cancer itself. No participant died.

What does this mean for trial patients?

Although there were not enough patients for the data to show a definite result, trial participants all were given the current best available treatment.

How will the results help patients and doctors in future?

When to have chemotherapy for bowel cancer that has spread to the liver is a very important question, but the three trials could not attract enough participants to answer it.

This was a concerning problem for the people conducting the trial. The investigators contacted the patients' own oncologists, and found that the oncologists would consider each patient individually and would select the treatment they thought was better. Medical specialists on three continents had indicated that they were interested in the topic of the trial, but then insufficient specialists were comfortable with randomisation for their patients, so did not enrol them in the trial, and the result was not enough participants.

What will the researchers do next?

The researchers are continuing to study the issue of not enough participants by sending detailed questionnaires to doctors asking about the treatment they prefer for hypothetical patients with various characteristics.

The aim is to analyse the answers to find out if there is a preference for the time of chemotherapy for certain kinds of patients and the reasons.

Where can I find out more about the trial?

Talk with your GP or oncologist.

The results have been presented at an international conference

Goldstein D, Fawcett J, and others. Safety and toxicity of peri-operative and post-operative adjuvant therapy for hepatic metastases from colorectal cancer: results from AGITG ATTACHE, CRUK EPOC-B and NSABP C-11. *European Cancer Congress 2015; Vienna*. Link to abstract. Search for Fawcett to find the detailed poster.

Trial registration

Australian New Zealand Clinical Trials Registry
www.anzctr.org.au
Search for number ACTRN12610000647033.

Australian Cancer Trials

www.australiancancertrials.gov.au

Australasian Gastro-Intestinal Trials Group

agitg.org.au/clinical-trials/completed-trials

The sponsor was the Australasian Gastro-Intestinal Trials Group (AGITG). The study was coordinated by the Clinical Trials Centre at the University of Sydney.

The study was funded by Cancer Australia and had no commercial funding. The investigators have no conflict of interest.

Results of any clinical trial do not represent complete knowledge about treatment. Patients should not change their therapy on their understanding of the results.